Respiratory system physiology

sheet | handout | slides

Number	9
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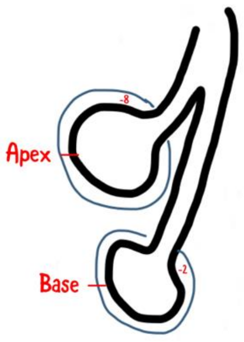
(Slides and their notes are added)

Closing Volume

Bronchioles are going to close when reaching a specific volume. This volume is the closing volume. It is a very sensitive test when there is no obstruction detected in the pulmonary function test for a heavily smoking patient.

At the beginning of inspiration, there is difference in the intraplural pressure between apical and basal alveoli, it is -8 , -2 respectively. This difference is what makes apical alveoli more inflated than basal alveoli at the beginning of inspiration, so we can say that-2 mmHg is the closing pressure for basal alveoli.



To measure the closing volume, we ask the patient to take 100% oxygen saturated FRC . Although most of the oxygen will go to the base , the first part of the inspired air will go to the apex. But always remember that most of ventilation goes to the base not the apex (you can't inflate an already inflated alveolus).

Steps:

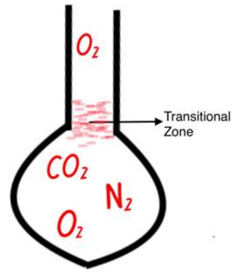
1) Ask the patient to inspire pure oxygen.
2) Ask the patient to exhale through a special tube which is connected to a machine that analyzes the N_2 in the exhaled air.
3) The machine will draw a chart for the **N_2 percentage** and **the volume of the exhaled air**. This is called the *Nitrogen Washout*

We previously mentioned that N_2 is present in the alveoli and we considered it and $H_2O_{(g)}$ as spectators. As most of pure oxygen will go down, the air in the basal alveoli will be more diluted in respect for N_2 meaning that P_AN_2 will be lower in basal alveoli.

In expiration and as bronchioles are going to close, *basal alveoli* will close *first* and the last part of the expiratory air is from apical bronchioles.
During expiration, the pressure becomes less negative. That may lead to compression and occlusion in the basal duct {narrower one}, before the apical {wider one}.

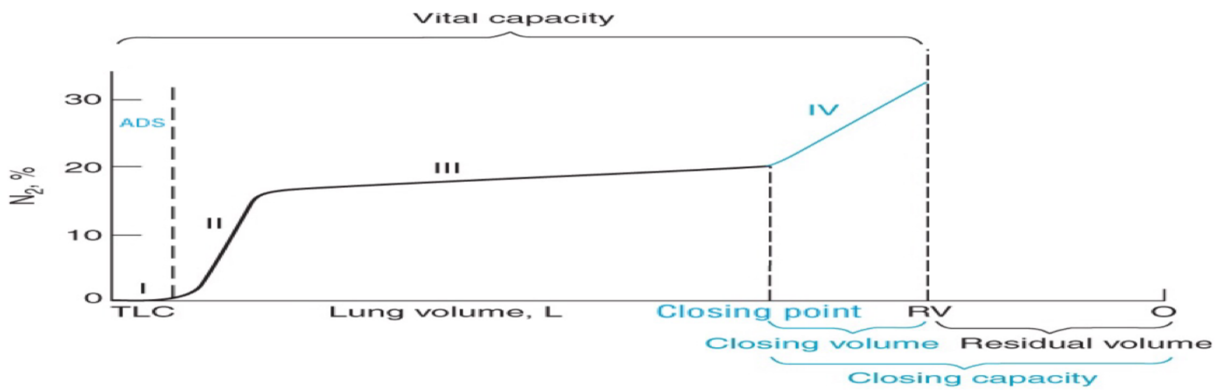
We can define the closing volume as the volume of air which is exhaled after the basal bronchioles close.

REM: In ADS , there is pure O_2 and no N_2 (since we are giving the patient pure oxygen now).



- There is a transitional zone where gases are exchanged and not a real cut of gas separation.
- In blood we have O_2 , N_2 , CO_2 , H^+ and the lungs make them stable in homeostasis.
- First part of the exhaled air is from the ADS so it doesn't contain nitrogen.

REM: Physiological dead space minimal volume is equal to ADS (alveolar wasted volume is zero in this case)



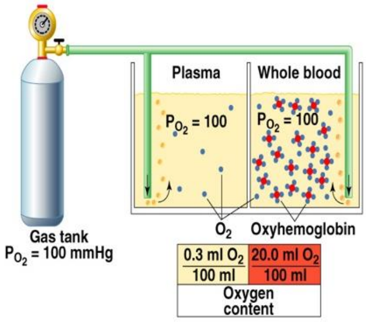
When basal alveoli close, air will be expired from the apical alveoli

In normal people, the closing point is at the residual volume. The closing volume will be zero meaning that the exhaled air is from both the apex and the base. In case of obstruction, the closing volume will **increase** (basal bronchi will close earlier) and air is mainly exhaled from the apex (this increase in volume is proportional to the degree of obstruction)

Measuring the closing volume will tell us if the patient has **obstruction** disease in addition to the degree of the obstruction. Also it is used to measure the **ADS**.

Oxygen in Blood

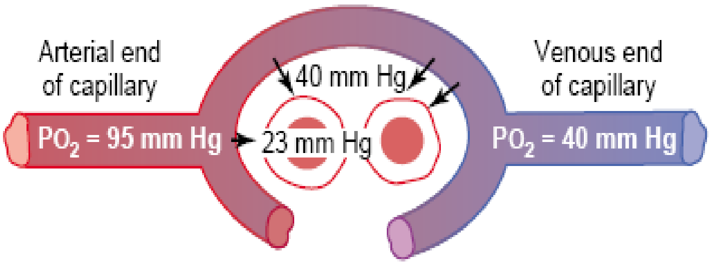
Oxygen can be **dissolved in plasma** (minimum) and bound to Hb in the RBCs as **oxyhemoglobin Hb-O_2**



- Blood volume is 7% of the body weight
- For a 70 kg person it is about 5L = 5000mL
- RBC= 5 million per µl blood
- 280 million Hb/RBC
- Each Hb has 4 polypeptide chains and 4 hemes
- In the center of each heme group is 1 atom of iron that can combine with 1 molecule of O_2
- The extraction ratio of oxygen by cells (what cells are going to utilize) is normally 25% (5mL/ 20mL *100% = 25%)
- 1g Hb can bind reversibly 1.34 mL of oxygen
  (15g/dL * 1.34mL/1g =20 mL/dL)
- In the plasma , we measure it as follows:
  $[O_2]$ = Solubility * P_aO_2
  = 0.003 * 100 = 0.3mL/dL blood

The total oxygen = 20 + 0.3 = 20 (we can ignore 0.3)

- Oxygen is always being used by the cells. Therefore , the intracellular PO_2 in the peripheral tissue cells remains lower than the PO_2 in the peripheral capillaries.

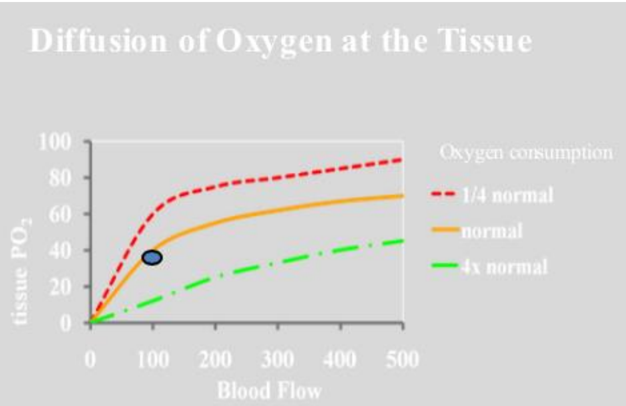


Increased Blood Flow to Tissues

- Normal blood flow
  - 200 ml O_2 / L ml blood * 5L blood/min= 1000 ml O_2 /min…250 ml are consumed at rest (25%)
- **Utilization Coefficient or (Extraction ratio):**
- Is the % of blood that gives up its O_2 as it passes through tissue capillaries. Normally is 25%. In exercise 75% - 85%. In some local tissues with extremely high metabolic rate → 100%.

O2 Uptake during Exercise

- VO_2 increases during exercise until it reaches V O_2 max…what limits VO_2 max…lung? CVS? number of mitochondria?
- Increased cardiac output, muscle blood flow and extraction ratio, all make more O_2 available to the exercising tissues
- This will result in decreased transit time (fast blood flow), but normal lungs can still oxygenate the blood.
- Increased diffusing capacity by:
  - Opening up of additional capillaries
  - Better ventilation/perfusion match
- Equilibration happen within shorter time.



- Arterial blood has PO_2 of 95-100 mmHg
- Tissue has a PO_2 of 30-40 mmHg
- Tissue PO_2 is determined by balance of delivery and usage.

Gas Content:

- Arterial Blood
  (PO_2 95 mm Hg;PCO_2 40 mm Hg;Hb 97% Saturated)
  - Venous Blood
    (PO_2 40 mm Hg;PCO_2 45 mm Hg;Hb 75% Saturated)

Oxygen Transport

- Partial Pressure (mm Hg)
  - driving force for diffusion
- Percent Saturation (no units)
  HbO_2
  ($Hb+O_2$) is called oxyHb
- Content (ml O_2/100 ml blood)
  - The absolute quantity of oxygen in the blood is the most important among others

- Henry's law
- Dissolved oxygen=PaO_2 X Solubility of O_2 Solubility 0.003 ml O_2/100 ml blood
- \- In normal blood; the [O_2] in its dissolved form is equal to= 0.3 ml O_2/100 ml blood
  - Normal oxygen consumption 250 ml O_2/min
  - Would require 83 l/min blood flow

Arterial blood

For venous blood, pressure will be 45mmHg and the dissolved oxygen = 45*0.003=0.135

- Hemoglobin
  - 97% of the transported O2 is in this form

$$O_2 + Hb \rightleftharpoons HbO_2$$

<u>Law of Dissolved Gases:</u>

Oxygen	0.024
Carbon dioxide	0.57
Carbon monoxide	0.018
Nitrogen	0.012
Helium	0.008

- Much more CO_2 is dissolved in blood than O_2 because CO_2 is 20 times more soluble.
- The air we breathe is mostly N_2, very little dissolves in blood due to its low solubility.

- Oxygen transport
  - Only about 1.5% is in the dissolved form (in plasma)
  - 98.5% bound to hemoglobin in red blood cells
    - Heme portion of hemoglobin contains 4 iron atoms – each can bind one O_2 molecule
    - Only dissolved portion can diffuse out of blood into cells
    - Oxygen must be able to love (bind, associate, load, increase affinity) and hate dissociate (hate, unload
    - decrease affinity).

Hemoglobin

Since the solubility of O_2 in blood is low then the amount transported, as dissolved O_2 is also low. Our body provides a mechanism for transporting O_2, the O_2 binding protein (Hb).

Hb Type	Description
Adult (A) HbA $\alpha_2\beta_2$	α = 141 β 146 M.W =64.460(<70k[1])
Fetal (P) HbF $\alpha_2\gamma_2$	2% of normal blood.
Sickle (S) Hb^S $\alpha_2\beta_2^S$	
Hb(A_2) $\alpha_2\delta_2$	2% of adult Hb.

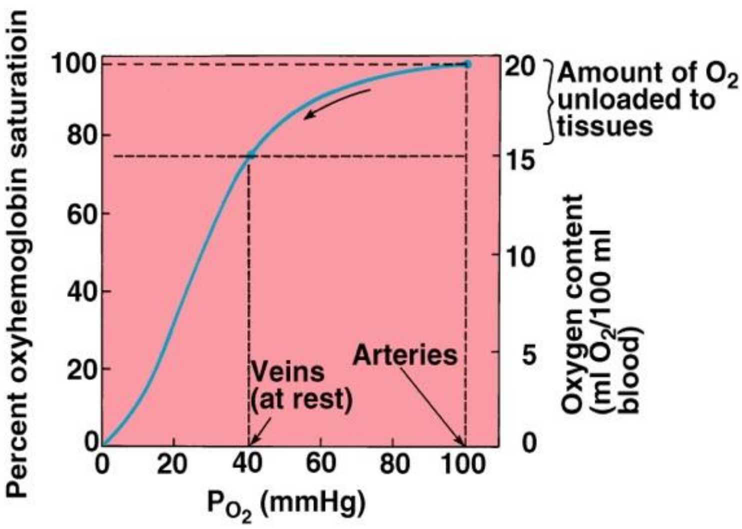
Hb is in its ferrous state F^{+2}, this can bind O_2 reversibly, but ferric Fe^{+3} is useless because it does not release O_2. NADH-meth-Hb reductase can convert ferric to ferrous form.

Hb: has 4 chains, each having heme group (iron – containing porphyrin rings)., which can bind one molecule of O_2.

Abbreviation	Indications
Hb	deoxygenated Hb or reduced Hb or ferrohemoglobin
HbO_2	oxy-Hb
Hb (ferric)	Oxidized or methHb . or ferrihemoglobin (1% of the total Hb).
HbCO	Carboxy-Hb.
$HbCO_2$	Carbamino-Hb.

[1] <70 means it can be filtered through the glomerulus so Hb may be seen in the urine ending with hemoglobinuria

- Oxyhemoglobin:
  - Normal heme contains iron in the reduced form (Fe^{2+}).
  - Fe^{2+} shares electrons and bonds with oxygen.
- Deoxyhemoglobin:
  - When oxyhemoglobin dissociates to release oxygen, the heme iron is still in the reduced form.
- Methemoglobin:
  - Has iron in the oxidized form (Fe^{+++}).
    - Blood normally contains a small amount. but ferric Fe^{+3} which is useless because it does not release O_2. NADH-meth-Hb reductase can convert ferric to ferrous form
- Carboxyhemoglobin:
  - The reduced heme is combined with carbon monoxide.
  - The bond with carbon monoxide is **250** times stronger than the bond with oxygen.
    - Therefore, transport of O_2 to tissues is impaired.
- Oxygen-carrying capacity of blood determined by its hemoglobin concentration.
  - Anemia:
    - [Hemoglobin] below normal.
  - Polycythemia:
    - [Hemoglobin] above normal.
  - Hemoglobin production controlled by erythropoietin.
    - Production is stimulated by the decrease in renal PO_2
- Loading/unloading depends:
  - PO_2 of environment.
  - Affinity between hemoglobin and O_2.



- Graphic illustration of the % oxyhemoglobin saturation at different values of PO_2.
  - Loading and unloading of O_2.
    - Steep portion of the sigmoidal curve, small changes in PO_2 produce large differences in % saturation (unload more O_2).
- Decreased pH, increased temperature, increased 2,3 DPG, and increase PCO_2 all will decrease affinity of hemoglobin for O_2 → greater unloading of O_2 → Shift of the Hb-O_2 dissociation curve to the right. Hb hates O_2 or the so called decrease affinity.

PO2	O2 sat	Notes
100 mmHg Arterial	100% 20 mL	Exceeding the 100% is not efficient so don't try to make the pressure >100mmHg The additional oxygen above the 100 is in the dissolved form not the bound, and it's not sufficient to make a change. If the PO_2 is more than 2000mmHg we theoretically won't need RBC but this amount of oxygen is toxic and cannot be achieved
60 mmHg	90% 18 mL	Ascending to high altitudes will decrease the atmospheric pressure , P_AO_2 and P_aO_2 The percentage of oxygen outside is always constant at 21% but PH_2O will be more with the same contribution of 47mmHg Any increased ascending will result in major changes and stimulation of the respiratory centers.
40 mmHg Venous	75% 15 mL	15 mL is what remains after cells extracts their needs (25% or 5 mL)
26 mmHg	50% 10 mL	P_{50} (%50 of the Hb is bound to O2)

The relation is not linear(although directly proportional), but rather **sigmoidal** due to the **allosteric effect**. If oxygen is present there is a higher chance of binding. In other words, for Hb to be saturated oxygen must be present in the plasma in sufficient amount.

Hb is an allosteric protein, so binding of first oxygen molecule will make the binding of the second easier and so on. Also binding of oxygen is affected by binding with CO_2 , CO , 2,3-BPG

By increasing the partial pressure of oxygen, the **dissolved** oxygen will increase.

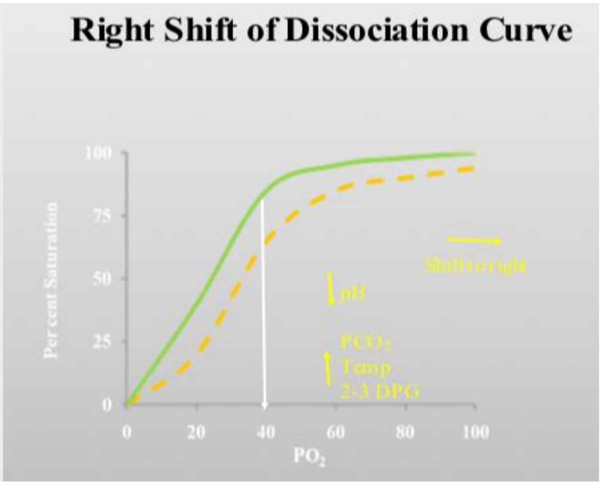
below **60** mmHg there is **a significant decrease in saturation**. Also hyperventilation will drive the pressure above 60 to decrease the PCO_2 and increase the PO_2. Control systems which are mainly sensitive for CO_2 will be stimulated if PO_2 is lower than 60 mmHg.

Hb we need must **love** and **hate** oxygen :

- Alveoli **High affinity**
  - Over wide range hemoglobin will be highly saturated
  - example: PO_2 of 60 mmHg correspond to 90% saturation

- Tissue **Low affinity**
  - Normal: consume 5 ml O_2/100 ml blood (P_iO_2 is 40 mmHg)
  - During exercise: 15 O_2 /100 ml blood (P_iO_2 is only 20 mmHg)

- Right shift occurs at tissue level…Bohr's effect
  - ↑$PaCO_2$ or ↑ arterial H^+→ ↓ affinity for oxygen or increase O_2 release…this occur at the tissue level
- Left shift at lungs…Haldane's effect is the reverse Bohr's effect
  - loss of carbon dioxide at lungs → ↑affinity of Hb towards oxygen



During exercise , muscles need to extract more oxygen so the curve will shift to the right to increase oxygen release by **decreasing Hb affinity**. This occurs by increasing **CO_2 , 2,3-BPG , temperature** or **H^+**.
-> Remember: O_2 and CO_2 **don't** compete on the same binding site on Hb.

Good Luck <3